SUPPLEMENTARY METHODS

Clinical Diagnosis of cHCL and vHCL: All study cases were reviewed clinically by American Board of Pathology-certified hematopathologists and diagnosed based on currently published morphological and immunophenotypic criteria used to distinguish cHCL ($CD20^+CD11c^+CD103^+CD25^+CD123^+CD200^+$) and vHCL ($CD20^+CD11c^+CD103^+CD25^-CD123^-CD200^-$).[1-5]

Isolation of genomic DNA: DNA was extracted from mononuclear cells and, in some cases, granulocytes following Ficoll separation of either bone marrow aspirates or peripheral blood versus germline control. For some cases, $CD19^+/CD103^+/CD11c^+$ selected cells were FACS-purified for DNA extraction along with the $CD19^-$ negative control fraction. DNA was isolated using a Qiagen Allprep DNA/RNA/Protein Mini Kit according to the manufacturer's protocol. After quality control of isolated DNA (gel electrophoresis and Agilent Bioanalyzer 2100), extracted nucleic acids were submitted to sequencing facilities.

MSK-IMPACT Variant Calling of Single Nucleotide Variants (SNVs), Indels, and Copy Alterations: When paired normal was available, we used paired-sample variant calling on tumor samples and their respective matched normal samples to identify point mutations/SNVs and small indels (<30 bp in length). When matched normal samples were not available, tumor samples were considered as unmatched samples, and variant calling was performed using a within-batch mixed normal control sample instead. MuTect (version 1.1.4) was used for SNV calling, and SomaticIndelDetector, a tool in GATK version 2.3.9, was used for detecting indel events. The following standard filters were applied to the raw MuTect and SomaticIndelDetector output as a first pass (with more rigorous filters being applied at a subsequent stage): variant frequency in tumor/variant frequency in normal >5x, number of mutant allele reads in tumor sample >5x, variant frequency in tumor sample >1%. Variants were annotated using Annovar (version 527), and the output was reformatted using a custom script to ensure annotations of the cDNA, and protein primary sequence changes are compliant with HGVS standards. Dinucleotide and trinucleotide substitutions identified by the pipeline were annotated manually because this functionality was not supported by the version of Annovar used. Only variant annotations relative to the canonical transcript for each gene (derived from a list of known canonical transcripts obtained from the UCSC Genome Browser) were reported. In cases where variant calling was performed using an unmatched normal sample, variants with minor allele frequency >1% in the 1000 Genomes cohort were removed[6]. Further filtering for high-confidence SNVs and indel calls prior to the final step of manual review included the following: evidence in the literature for being an oncogenic or recurrent hotspot mutation; whether or not these were reproducible assay artifacts with occurrence of the variant in previously run pools of normal controls; technical characteristics (depth of coverage, number of mutant reads supporting the variant, and variant frequency); and whether or not the variant was exonic and nonsynonymous.[6-8]

Copy Number Analysis: Copy number aberrations were identified by comparing sequence coverage of targeted regions in a tumor sample relative to a standard diploid normal sample, following a Loess-normalization to adjust for the dependency of coverage on GC content across all samples studied here as previously described.[6-8] Significant exon- and gene-level copy number gains and losses were inferred using the following tumor:normal sequence coverage ratio criteria: fold change ≥2.0 (gain) or ≤2.0 (loss), $p<0.05$ (false discovery rate corrected for multiple testing).

In addition to the above methods (which represent our standard coverage-based copy number pipeline for MSK-IMPACT data used in numerous publications to date[6-16]), arm and

chromosome level alterations were confirmed by a separate copy number alteration detection algorithm known as FACETS.[17] Here, Loess regression was used to correct for GC bias over 1kb windows along the genome. Joint segmentation of total copy number log-ratio (logR) and allelic log-odds-ratio (logOR) was performed based on a bivariate Hotelling T2 statistic. Any positional shift of the 2-copy state from zero detected due to aneuploidy of the tumor was quantified and used to estimate tumor ploidy. In the final step, integer copy number and associated cellular fraction were estimated using a Gaussian non-Central Chi-Square mixture model. Tumor purity was inferred from the cellular fraction estimates.

Fluorescence in situ Hybridization (FISH): Commercially available probes LSI 7q31, LSI CEP7, and LSI 13q14.3/LSI 13q34 (VYSIS, Inc.) were utilized. The probes were hybridized on 5µm-thick tissue sections, and the number and localization of the hybridization signals were assessed in a minimum of 100 interphase nuclei. Probes were co-denatured with the target cells on a slide moat at 90°C for 12 minutes. The slides were incubated overnight at 37°C on a slide moat and then washed in 4M Urea/2xSSC at 25°C for 1 minute. Nuclei were counterstained with DAPI (200ng/ml)(Vector Labs). Images were captured and processed using the Cytovision v7.3 software from Leica Biosystems (Richmond, IL).

RNA Interference by Short Hairpin RNA (shRNA) and Drug Studies: Custom *de novo* shRNA were generated on the miR-E backbone and cloned into the pLENC retroviral vector by the MSKCC RNAi core facility as described previously[18]. The sequences used are shown below:

shRNA name	Antisense Sequence
Nf1_1816	TTAAGAAGAAATTTATTTCTGC
Nf1_3353	TTCATCTTCAACTTCACTACAG
Nf1_6884	TTTTGTTAGTGCTATCACCGTA
Nf2_1438	TTTTCTTTCTCTATCTCCATGG

Murine Ba/F3 cells stably expressing *BRAF* V600E-GFP were infected with retrovirus containing shRNA constructs targeting either a control (Renilla luciferase) or murine *Nf1* or *Nf2* and also expressing mCherry and a Neomycin resistance gene. After negative selection in antibiotic containing media, GFP/mCherry double positive cells were sorted by FACS and *Nf1/Nf2* gene expression was measured by Taqman quantitative RT-PCR (Applied Biosystems). These cells were also tested for sensitivity to PLX-4720, a potent inhibitor of BRAFV600E. Half-maximal inhibitory concentrations were determined by measuring cell viability after 72 hours of treatment via the CellTiter-Glo ATP luminescence assay (Promega) and calculated using GraphPad Prism v6.0 software.

Western Blotting: Anti-IRS-1 (no.2382), anti-phospho-p44/42 MAPK (ERK1/2) (Thr202/Tyr204) (no. 9101), anti-p44/42 MAPK (ERK1/2) (137F5) (no.4695), anti-phospho-AKT (Ser473) (no.9271), anti-AKT (C67E7) (no.4691), as well as the secondary antibodies anti-rabbit IgG-HRP (no. 7076) and anti-mouse IgG-HRP (no. 7074) were purchased from Cell Signaling Technology. Anti-β-Actin (A5441) was purchased from Sigma-Aldrich®. Cell lysates were prepared in RIPA buffer supplemented with Halt protease and phosphatase inhibitor cocktail (Thermo Scientific). Equal amounts of protein, as measured by the BRADFORD

protein assay, were resolved in 4–12% Bis-Tris NuPage gradient gels (Life Technologies) and transferred electrophoretically on a polyvinylidene difluoride 0.45-m membrane. Membranes were blocked for 30 minutes at room temperature in 5% bovine serum albumin (BSA) in TBST before being incubated overnight at 4°C with the primary antibodies. All primary antibodies were diluted 1:1,000 in 5% BSA in TBST, except anti-β-actin, which was diluted 1:5,000 in 5% BSA in TBST. After three washes of 5 min in TBST, secondary antibodies were diluted 1:2,000 in 5% BSA in TBST and incubated for 1 h at room temperature. After another three washes in TBST, detection of the signal was achieved by incubating the membrane on an ECL solution from Millipore and exposure on autoradiography films from Denville Scientific (Metuchen, NJ, USA).

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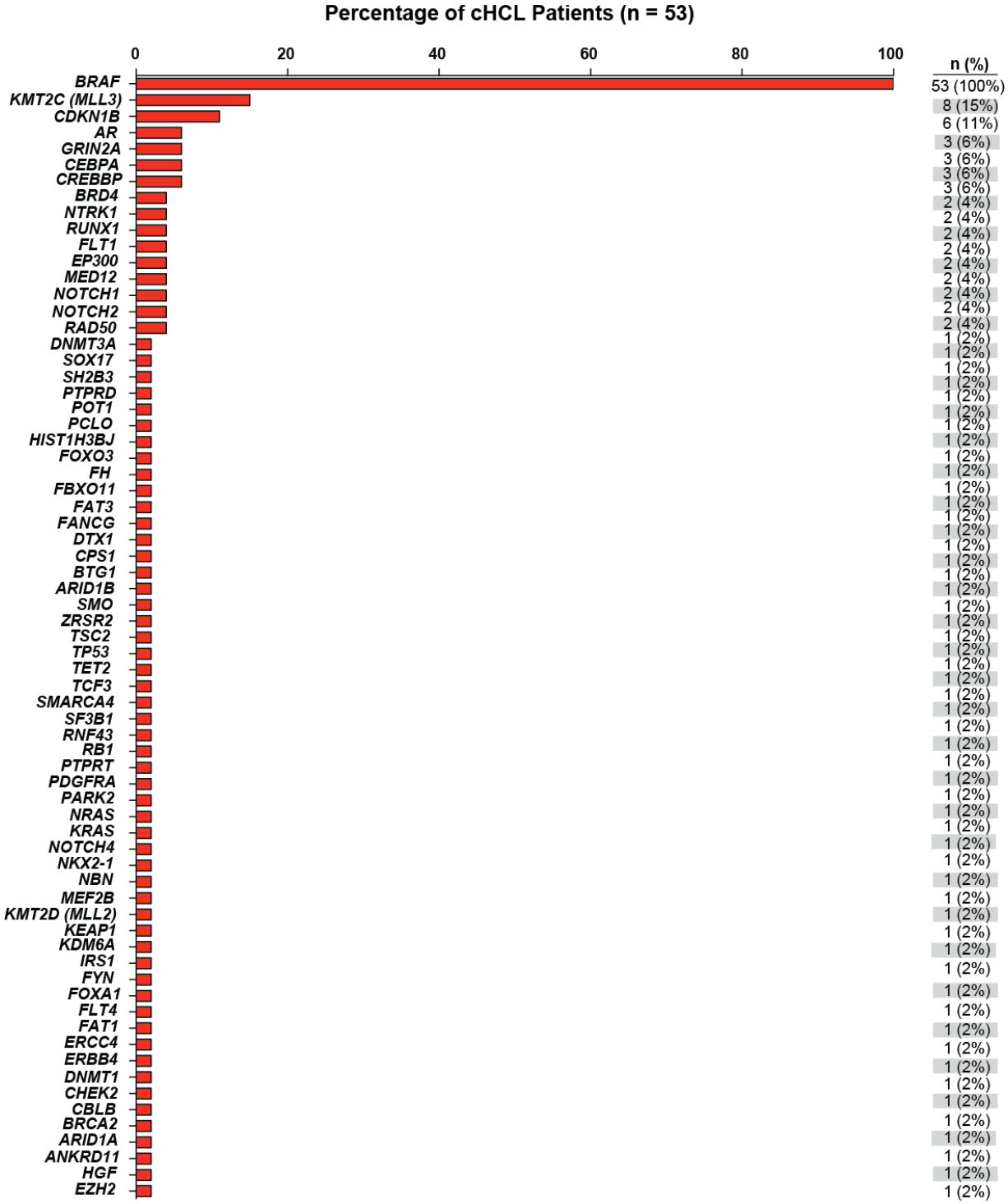
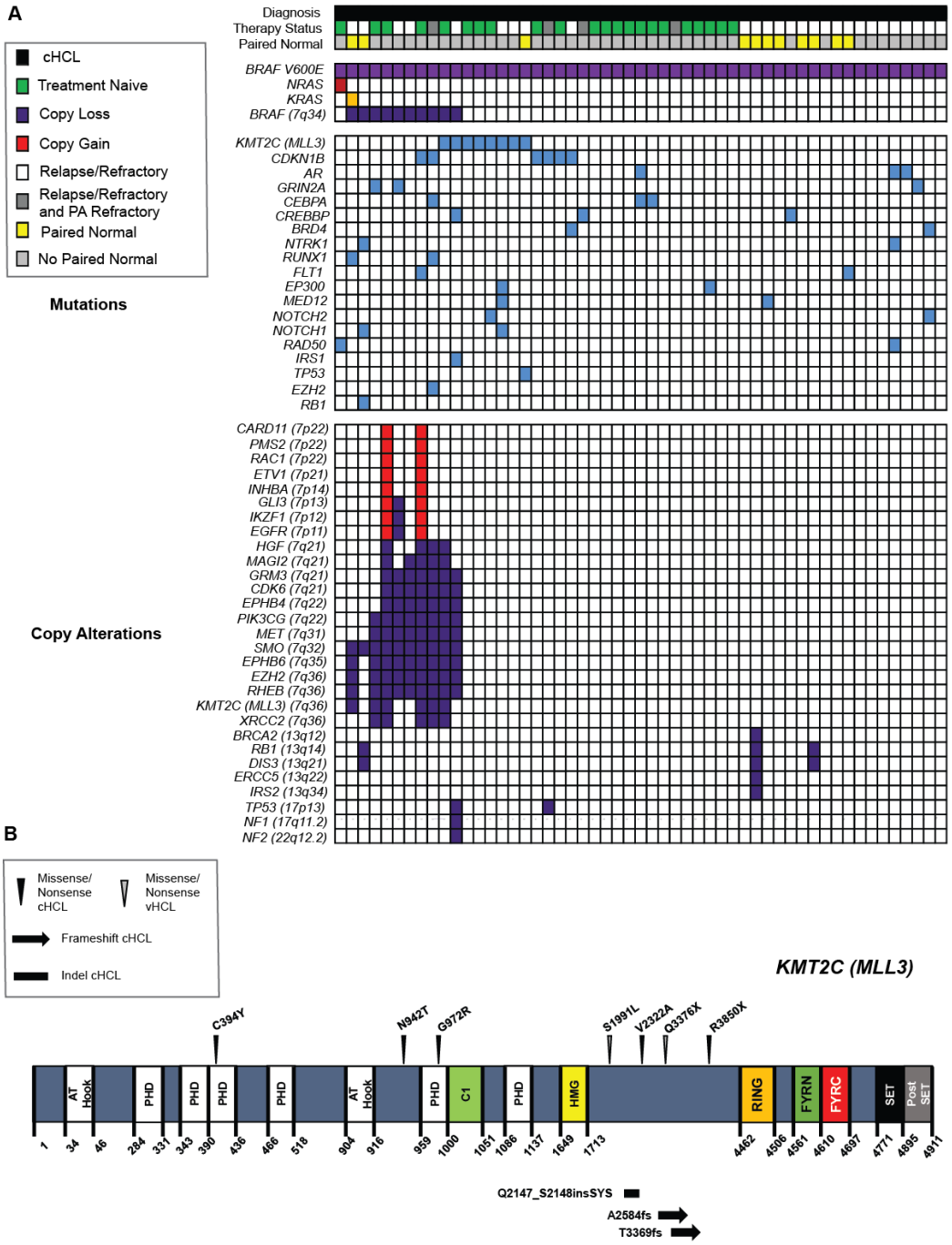
Supplementary Figure 1. Histogram of mutations in cHCL cohort (n=53 patients) across all patients evaluated by targeted-capture next-generation sequencing.



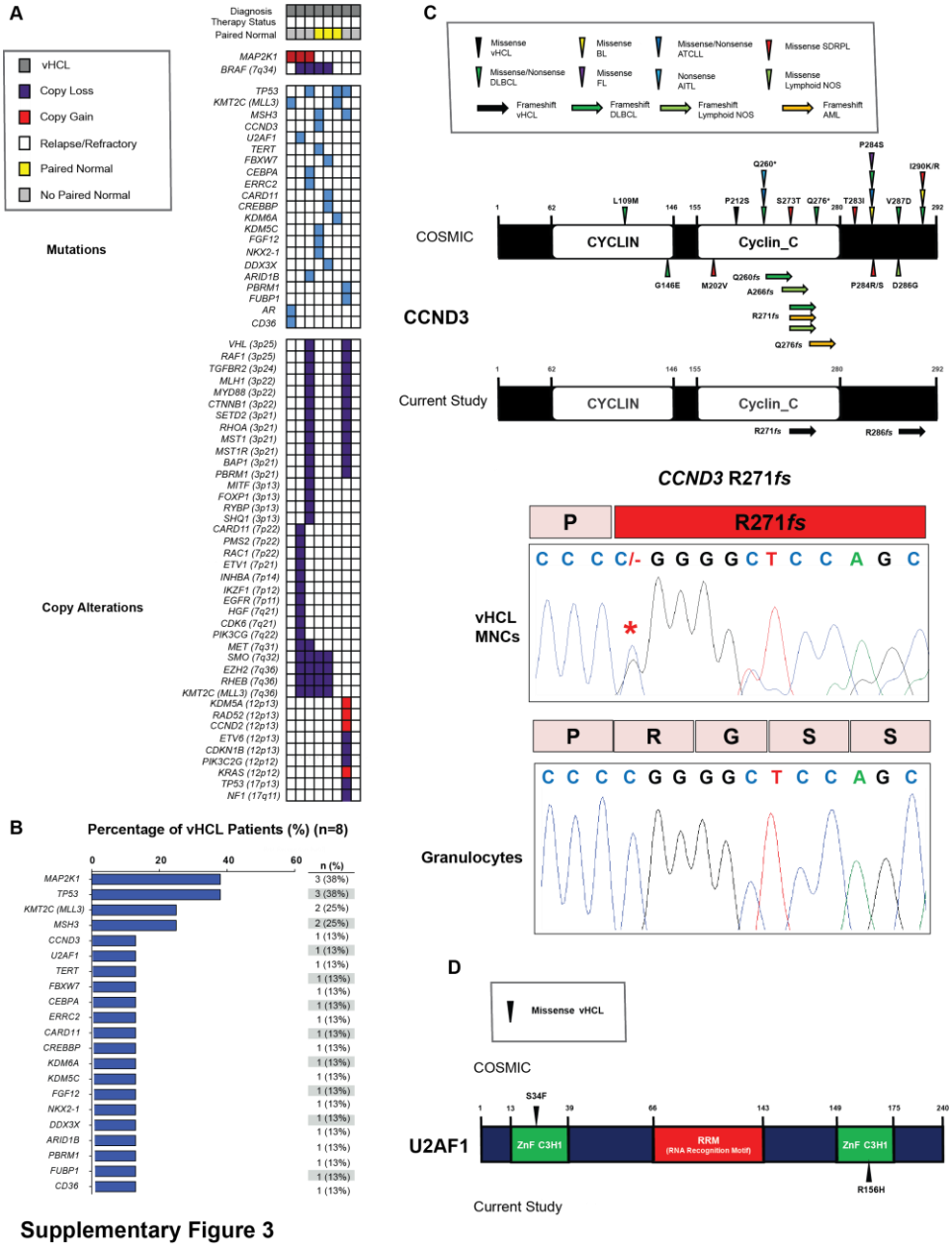
Supplementary Figure 1

Supplementary Figure 2. Somatic mutations in cHCL. (A) Heat map of all recurrent and selected non-recurrent mutations and copy number alteration in cHCL. Each patient is represented in one column. The cHCL diagnosis, therapy status (treatment naïve, relapse/refractory, and relapse/refractory and purine analog refractory), and paired normal status are in the first 3 rows. Selected somatic mutations and copy alterations are in subsequent rows. **(B)** Diagram of *KMT2C (MLL3)* mutations identified in this study.



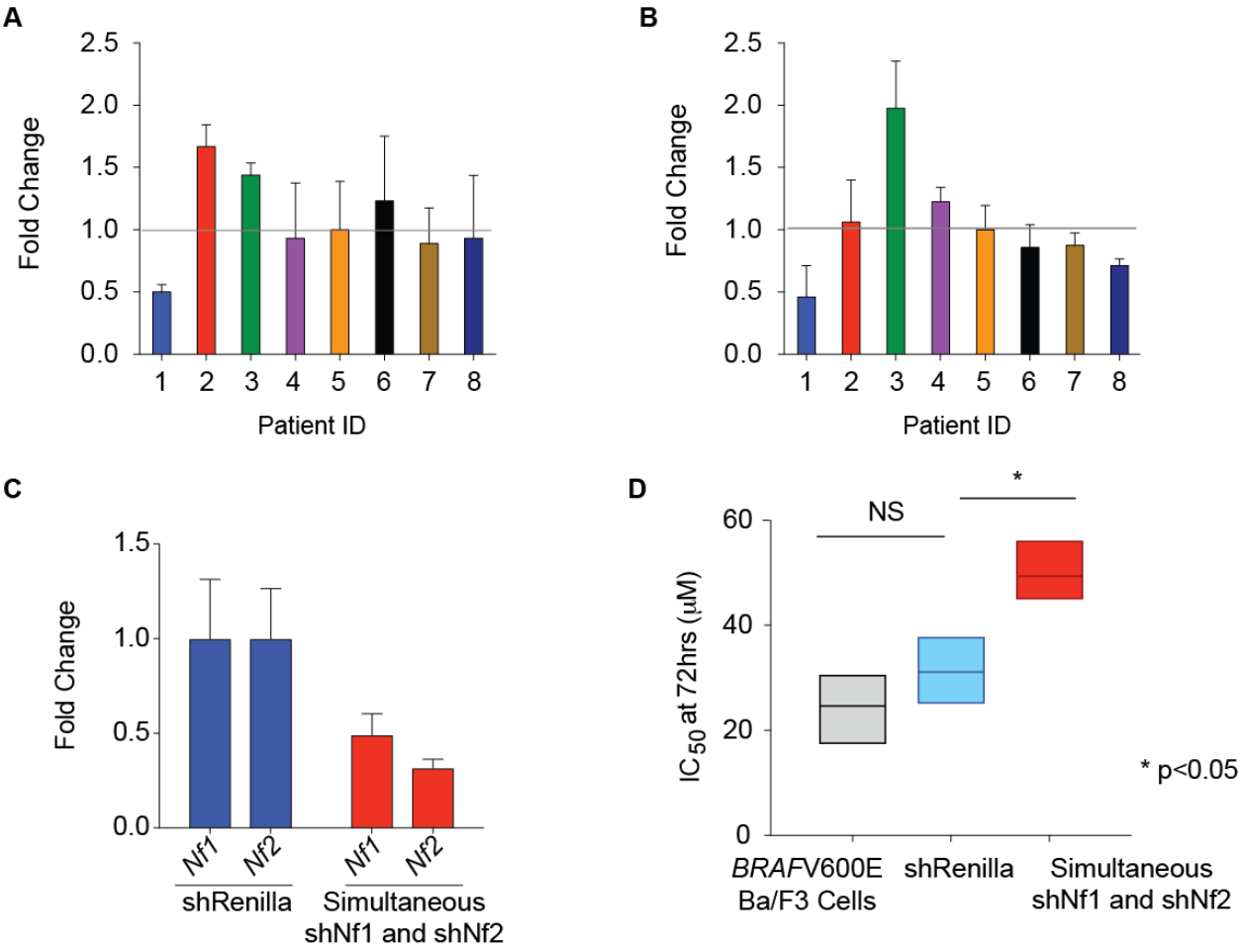
Supplementary Figure 2

Supplementary Figure 3. Somatic mutations in variant HCL (vHCL). **(A)** Heat map of somatic mutations and selected copy number alterations in vHCL from study cohort. Each patient is represented in one column. vHCL diagnosis, therapy status (relapse/refractory), and paired normal status are in the first 3 rows. Somatic mutations and selected copy alterations are in subsequent rows. **(B)** Histogram of mutations in vHCL cohort (n=8) patients from current study). **(C)** Diagram of *CCND3* confirmed somatic mutations identified in hematopoietic malignancies in COSMIC (**top**) and variant HCL from the current study (**bottom**) with Sanger sequencing electropherograms demonstrating *CCND3* p.R271fs mutation in vHCL cells and not in paired normal granulocytes. **(D)** Diagram of *U2AF1* confirmed somatic mutations identified in variant HCL from COSMIC (**top**) and this study (**bottom**).



Supplementary Figure 3

Supplementary Figure 4. *In vitro* studies of *NF1/2* loss and vemurafenib resistance. (A) qRT-PCR of human (h) *hNF1* expression in patient samples of a *de novo* vemurafenib-resistant patient with heterozygous copy loss of *NF1* (patient 1) and patients with no copy loss of *NF1* (patients 2-8). **(B)** qRT-PCR of human (h) *hNF2* expression in patient samples of a *de novo* vemurafenib-resistant patient with heterozygous copy loss of *NF2* (patient 1) and patients with no copy loss of *NF2* (patients 2-8). **(C)** qRT-PCR of *Nf1* and *Nf2* expression following simultaneous anti-*Nf1*/*Nf2* shRNA knockdown. **(D)** IC_{50} of *BRAF*V600E-expressing Ba/F3 cells to vemurafenib with or without partial knockdown of *Nf1* and *Nf2* simultaneously.



Supplementary Figure 4

Supplementary Table 1. List of genes evaluated in the MSK-HemePACT assay.

(Please see separate Excel File)

Supplementary Table 2. Mutations identified in classical Hairy Cell Leukemia (cHCL).

Case	Case Cohort	Gene	Genomic Coordinates	Genomic Variant	Amino Acid Variant	VAFs	cHCL (%)	Paired Normal
OA-hcl-001-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	97.5%	100%	No
OA-hcl-001-P	Relapse/Refractory	*CREBBP*	chr16:3779038	c.6010C>T	p.R2004X	28.4%	100%	No
OA-hcl-001-P	Relapse/Refractory	*IRS1*	chr2:227659854	c.3601C>T	p.P1201S	10.2%	100%	No
OA-hcl-001-P	Relapse/Refractory	*KDM6A*	chrX:44733180	c.173_206del34	p.G58fs	1.8%	100%	No
OA-hcl-001-P	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151856070	c.11548C>T	p.R3850X	5.9%	100%	No
OA-hcl-003-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	75.7%	67%	Yes
OA-hcl-003-P	Relapse/Refractory	*NOTCH1*	chr9:139402414	c.3503C>T	p.S1168F	40.2%	67%	Yes
OA-hcl-003-P	Relapse/Refractory	*NTRK1*	chr1:156843643	c.1069G>A	p.G357S	43.9%	67%	Yes
OA-hcl-003-P	Relapse/Refractory	*RB1*	chr13:48951141	c1304_1331del28	p.G435fs	27.1%	67%	Yes
OA-hcl-004-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	15.5%	80%	Yes
OA-hcl-004-P	Relapse/Refractory	*CBLB*	chr3:105459399	c.891delT	p.I297fs	2.6%	80%	Yes
OA-hcl-006-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	37.6%	80%	Yes
OA-hcl-006-P	Relapse/Refractory	*SF3B1*	chr2:198267484	c.1873C>T	p.R625C	35.7%	80%	Yes
OA-hcl-007-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	2.4%	70%	Yes
OA-hcl-007-P	Relapse/Refractory	*DNMT1*	chr19:10247772	c.4430C>T	p.S1477F	0.13%	70%	Yes
OA-hcl-007-P	Relapse/Refractory	*MED12*	chrX:70349244	c.3656C>T	p.A1219V	3.0%	70%	Yes
OA-hcl-007-P	Relapse/Refractory	*TET2*	Chr4:106156992	c.1882delC	p.S631fs	13.2%	70%	Yes
OA-hcl-009-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	1.9%	15%	Yes
OA-hcl-010-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	79.5%	72%	Yes
OA-hcl-010-P	Relapse/Refractory	*KRAS*	chr12:25398284	c.35G>A	p.G12D	15.2%	72%	Yes
OA-hcl-010-P	Relapse/Refractory	*KRAS*	chr12:25378647	c.351A>T	p.K117N	1.2%	72%	Yes
OA-hcl-010-P	Relapse/Refractory	*RUNX1*	chr21:36259327	c.164C>A	p.A55E	6.0%	72%	Yes
OA-hcl-011-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	3.8%	75%	Yes
OA-hcl-011-P	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151962126	c.1181G>A	p.C394Y	6.7%	75%	Yes
OA-hcl-011-P	Relapse/Refractory	*NOTCH1*	chr9:139418204	c.368C>T	p.T123M	50.6%	75%	Yes
OA-hcl-011-P	Relapse/Refractory	*EP300*	chr22:41574281	c.6568del12	p.Q2192_Q2195del	35.7%	75%	Yes
OA-hcl-011-P	Relapse/Refractory	*MED12*	chrX:70360623	c.6182_6185delAAC	p.2061_2062QQ>Q	6.4%	75%	Yes
OA-hcl-012-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	77.0%	70%	No
OA-hcl-012-P	Relapse/Refractory	*GRIN2A*	chr16:9943692	c.1249G>A	p.V417I	45.9%	70%	No
OA-hcl-012-P	Relapse/Refractory	*ARID1A*	chr1:27100999	c.4281delA	p.V1427fs	2.9%	70%	No
OA-hcl-013-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	13.1%	10%	No
OA-hcl-013-P	Relapse/Refractory	*CREBBP*	chr16:3778500	c.6548C>T	p.A2183V	46.8%	10%	No
OA-hcl-016-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	2.8%	60%	Yes
OA-hcl-017-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	0.6%	80%	Yes
OA-hcl-020-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	47.4%	70%	No
OA-hcl-021-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	43.6%	61%	Yes
OA-hcl-021-P	Relapse/Refractory	*PTPRT*	chr20:40730876	c.3659G>A	p.R1220Q	48.4%	61%	Yes
OA-hcl-021-P	Relapse/Refractory	*SMARCA4*	chr19:11138480	c.3236C>T	p.S1079L	46.7%	61%	Yes
OA-hcl-023-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	0.3%	98%	Yes
OA-hcl-023-P	Relapse/Refractory	*FLT1*	chr13:29004241	c.1052G>A	p.R351Q	0.2%	98%	Yes
OA-hcl-026-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	4.9%	20%	No
OA-hcl-026-P	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151927070	c.2914G>C	p.G972R	9.4%	20%	No
OA-hcl-026-P	Relapse/Refractory	*PDGFRA*	chr4:54245413	c.160_162delGAA	p.E54del	40.1%	20%	No
OA-hcl-037-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	11.4%	90%	Yes
OA-hcl-037-P	Relapse/Refractory	*FAT1*	chr4:187542275	c.5465T>G	p.I1822S	9.0%	90%	Yes
OA-hcl-037-P	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151927351	c.2825A>C	p.N942T	15.7%	90%	Yes
OA-hcl-037-P	Relapse/Refractory	*TP53*	chr17:7578400	c.530C>T	p.P177L	4.6%	90%	Yes
OA-hcl-048-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	77.3%	80%	No
OA-hcl-050-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	3.8%	30%	No
OA-hcl-051-P	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	2.9%	80%	No
OA-hcl-501-P	Relapse/Refractory and PA Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	14.7%	36%	No
OA-hcl-501-P	Relapse/Refractory and PA Refractory	*CREBBP*	chr16:3801726	c.3779+1G>A	NA	11.6%	36%	No
OA-hcl-502-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	26.8%	30%	No
OA-hcl-502-P	Treatment Naïve	*FOXA1*	chr14:38061099	c.890C>T	p.P297L	48.2%	30%	No
OA-hcl-502-P	Treatment Naïve	*MEF2B*	chr19:19256726	c.986delG	p.G329fs	20.8%	30%	No
OA-hcl-502-P	Treatment Naïve	*CDKN1B*	chr12:12871105	c.333_351del19	p.G111fs	15.9%	30%	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	35.2%	18%	No
OA-hcl-503-P	Relapse/Refractory	*CDKN1B*	chr12:12870953	c.180G>A	p.W60X	38.1%	18%	No

	and PA Refractory							
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*CDKN1B*	chr12:12871011	c.238G>C	p.E80Q	34.7%	18%	No
OA-hcl-504-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	44%	86%	No
OA-hcl-505-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	46.8%	43%	No
OA-hcl-505-P	Treatment Naïve	*NOTCH4*	chr6:32163799	c.5427A>C	p.Q1809H	45.9%	43%	No
OA-hcl-505-P	Treatment Naïve	*CEBPA*	chr19:33792731	c.589_590insACCCGC	p.P197_P198insHP	24.2%	43%	No
OA-hcl-506-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	34.4%	29%	No
OA-hcl-506-P	Treatment Naïve	*KMT2D (MLL2)*	chr12:49427265	c.11222_11223insGCA	p.Q3741_Q3742insQ	27.7%	29%	No
OA-hcl-506-P	Treatment Naïve	*KEAP1*	chr19:10597342	c.1858_1860delCAG	p.620_620del	43.0%	29%	No
OA-hcl-507-P	Relapse/Refractory and PA Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	19.8%	40%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	92.1%	96%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*EZH2*	chr7:148516705	c.982C>T	p.Q328X	7.3%	96%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*RUNX1*	chr21:36206711	c.801G>A	p.M267I	61.5%	96%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*CEBPA*	chr19:33792731	c.589_590insACCCGC	p.P197_P198insHP	21.5%	96%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*EZH2*	chr7:148514988	c.1217_1220delAAGA	p.K406fs	8.2%	96%	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*CDKN1B*	chr12:12871782	c.500delC	p.A167fs	46.0%	96%	No
OA-hcl-509-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	88.0%	74%	No
OA-hcl-509-P	Treatment Naïve	*NBN*	chr8:90983470	c.633T>A	p.D211E	49.3%	74%	No
OA-hcl-510-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	81.0%	47%	No
OA-hcl-510-P	Treatment Naïve	*GRIN2A*	chr16:9862754	c.2549C>T	p.T850M	42.0%	47%	No
OA-hcl-511-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	71.0%	68%	No
OA-hcl-511-P	Treatment Naïve	*KMT2C (MLL3)*	chr7:151860554	c.10106_10107delCA	p.T3369fs	64.8%	68%	No
OA-hcl-512-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	8.7%	27%	No
OA-hcl-512-P	Treatment Naïve	*HGF*	chr7:81392144	c.133T>C	p.S45P	8.7%	27%	No
OA-hcl-513-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	26.5%	26%	No
OA-hcl-513-P	Treatment Naïve	*ZRSR2*	chrX:15841230	c.1314_1315insAGCCGG	p.G438_S439insSR	21.1%	26%	No
OA-hcl-514-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	42.9%	25%	No
OA-hcl-514-P	Treatment Naïve	*PARK2*	chr6:161771139	c.1390G>A	p.D464N	47.9%	25%	No
OA-hcl-514-P	Treatment Naïve	*TSC2*	chr16:2114392	c.1564_1566delCAC	p.522_522del	45.6%	25%	No
OA-hcl-515-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	11.2%	49%	No
OA-hcl-515-P	Treatment Naïve	*FYN*	chr6:112041022	c.233C>G	p.T78R	47.2%	49%	No
OA-hcl-515-P	Treatment Naïve	*RNF43*	chr17:56439937	c.655C>T	p.R219C	50.4%	49%	No
OA-hcl-515-P	Treatment Naïve	*CHEK2*	chr22:29092947	c.1037G>A	p.R346H	47.7%	49%	No
OA-hcl-515-P	Treatment Naïve	*TCF3*	chr19:1621907	c.882_884delCTC	p.294_295del	42.9%	49%	No
OA-hcl-516-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	9.7%	27%	No
OA-hcl-516-P	Treatment Naïve	*CEBPA*	chr19:33792731	c.589_590insACCCGC	p.P197_P198insHP	20.8%	27%	No
OA-hcl-516-P	Treatment Naïve	*AR*	chrX:66766350	c.1362_1363insGGT	p.G454_G455insG	39.6%	27%	No
OA-hcl-516-P	Treatment Naïve	*NKX2-1*	chr14:36986875	c.813_814insGGCGGGGGC	p.T272_G273insGGG	12.5%	27%	No
OA-hcl-517-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	39.7%	44%	No
OA-hcl-517-P	Treatment Naïve	*CDKN1B*	chr12:12871249	c.475+1G>T	NA	42.0%	44%	No
OA-hcl-517-P	Treatment Naïve	*CDKN1B*	chr12:12871879	c.596A>C	p.*199S	19.1%	44%	No
OA-hcl-517-P	Treatment Naïve	*ANKRD11*	chr16:89348451	c.4475_4498del24	p.1492_1500del	15.0%	44%	No
OA-hcl-518-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	42.4%	68%	No
OA-hcl-519-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	19.6%	21%	No
OA-hcl-519-P	Treatment Naïve	*BRCA2*	chr13:32929057	c.7068_7069delTC	p.F2356fs	48.2%	21%	No
OA-hcl-519-P	Treatment Naïve	*EP300*	chr22:41574340	c.6626_6637del11	p.2209_2213del	35.3%	21%	No
OA-hcl-520-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	17.3%	31%	No

OA-hcl-521-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	25.7%	59%	No
OA-hcl-521-P	Treatment Naïve	*KMT2C (MLL3)*	chr7:151878506	c.6438_6439insTCTTATTCC	p.Q2147_S2148insSYS	26.0%	59%	No
OA-hcl-522-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	46.2%	18%	No
OA-hcl-522-P	Treatment Naïve	*FLT4*	chr5:180053237	c.1132C>T	p.R378C	44.6%	18%	No
OA-hcl-522-P	Treatment Naïve	*CDKN1B*	chr12:12871054	c.281C>T	p.P94L	48.8%	18%	No
OA-hcl-522-P	Treatment Naïve	*FLT1*	chr13:28964199	c.1703C>T	p.T568M	48.6%	18%	No
OA-hcl-522-P	Treatment Naïve	*ERCC4*	chr16:14020606	c.578_583delGGCCAA	p.193_195del	36.0%	18%	No
OA-hcl-523-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	39.9%	65%	No
OA-hcl-523-P	Treatment Naïve	*KMT2C (MLL3)*	chr7:151874771	c.7750_7766del17	p.A2584fs	27.0%	65%	No
OA-hcl-524-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	28.0%	45%	No
OA-hcl-524-P	Treatment Naïve	*KMT2C (MLL3)*	chr7:151877980	c.6965T>C	p.V2322A	50.3%	45%	No
OA-hcl-524-P	Treatment Naïve	*NOTCH2*	chr1:120612002	c.17_18delCC	p.P6fs	17.1%	45%	No
OA-hcl-525-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	41.6%	26%	No
OA-hcl-525-P	Treatment Naïve	*ERBB4*	chr2:212566730	c.1451G>A	p.R484K	38.7%	26%	No
OA-hcl-527-P	Treatment Naïve	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	2.4%	6%	No
OA-hcl-527-P	Treatment Naïve	*NRAS*	chr1:115258748	c.34G>T	p.G12C	4.6%	6%	No
OA-hcl-527-P	Treatment Naïve	*DNMT3A*	chr2:25457176	c.2711C>T	p.P904L	9.5%	6%	No
OA-hcl-527-P	Treatment Naïve	*RAD50*	chr5:131976441	c.3696G>C	p.E1232D	8.3%	6%	No
OA-hcl-540-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	27%	70%	No
OA-hcl-540-T	Relapse/Refractory	*CDKN1B*	chr12:28709521	c.179G>A	p.W60X	25%	70%	No
OA-hcl-540-T	Relapse/Refractory	*CDKN1B*	chr12:28709521	c.179G>A	p.W60X	25%	70%	No
OA-hcl-540-T	Relapse/Refractory	*POT1*	chr7:124510987	c.233T>C	p.I78T	51%	70%	No
OA-hcl-540-T	Relapse/Refractory	*FBXO11*	chr2:48132690	c.169_170insAGC	p.P57_P58insQ	24%	70%	No
OA-hcl-540-T	Relapse/Refractory	*FOXO3*	chr6: 108882439	c.29_30delCG	p.P10*fs*	19%	70%	No
OA-hcl-540-T	Relapse/Refractory	*BRD4*	chr19:15354015	c.2864dupC	p.P955fs	16%	70%	No
OA-hcl-542-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	9%	25%	No
OA-hcl-542-T	Relapse/Refractory	*DTX1*	chr12:113532694	c.1328G>A	p.R443H	50%	25%	No
OA-hcl-542-T	Relapse/Refractory	*SMO*	chr7:128829039-128829040	c.47_48insGCT	p.G16_L17insL	35%	25%	No
OA-hcl-543-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	9%	11%	No
OA-hcl-543-T	Relapse/Refractory	*BTG1*	chr12:92539209	c.103C>T	p.R35X	9%	11%	No
OA-hcl-543-T	Relapse/Refractory	*NTRK1*	chr1:156851381	c.2339G>A	p.R780Q	51%	11%	No
OA-hcl-543-T	Relapse/Refractory	*PTPRD*	chr9:8486278	c.2539G>T	p.V847L	47%	11%	No
OA-hcl-543-T	Relapse/Refractory	*AR*	chrX:66765219	c.231_239delGCAGCAGCA	p.Q78_Q80del	18%	11%	No
OA-hcl-543-T	Relapse/Refractory	*RAD50*	chr5:131976441	c.3696G>T	p.E1232D	10%	11%	No
OA-hcl-544-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	15%	1%	No
OA-hcl-544-T	Relapse/Refractory	*HIST1H2BJ*	chr6: 27100519	c.11C>T	p.P4L	48%	1%	No
OA-hcl-544-T	Relapse/Refractory	*AR*	chrX:67545316-67545317	c.170_171GCAGCA	p.Q80dup	17%	1%	No
OA-hcl-544-T	Relapse/Refractory	*PCLO*	chr7:83134755	c.2795T>C	p.F932S	51%	1%	No
OA-hcl-545-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	10%	15%	No
OA-hcl-545-T	Relapse/Refractory	*GRIN2A*	chr16:9934644	c.1511G>A	p.R504Q	51%	15%	No
OA-hcl-545-T	Relapse/Refractory	*CPS1*	chr2: 211541733	c.4278delG	p.L1426fs	50%	15%	No
OA-hcl-545-T	Relapse/Refractory	*FAT3*	chr11:92592376	c.11546G>A	p.R3849Q	46%	15%	No
OA-hcl-545-T	Relapse/Refractory	*FH*	chr1:241661227	c.1433_1434insAAA	p.N478_G479insK	40%	15%	No
OA-hcl-546-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	2%	10%	No
OA-hcl-546-T	Relapse/Refractory	*BRD4*	chr19:15354015	c.2864dupC	p.P955*fs*	15%	10%	No
OA-hcl-546-T	Relapse/Refractory	*NOTCH2*	chr1: 120465265	c.4996G>A	p.V1666I	50%	10%	No
OA-hcl-546-T	Relapse/Refractory	*FANCG*	chr9: 35078617	c.292C>T	p.R98W	49%	10%	No
OA-hcl-546-T	Relapse/Refractory	*SOX17*	chr8:55372258	c.948_949CACCAG	p.Q324_H325dup	27%	10%	No
OA-hcl-547-T	Relapse/Refractory	*BRAF*	chr7:140453136	c.1799A>T	p.V600E	15%	15%	No
OA-hcl-547-T	Relapse/Refractory	*SH2B3*	chr12:111856571	c.622G>C	p.E208Q	56%	15%	No
OA-hcl-547-T	Relapse/Refractory	*ARID1B*	chr6:157100396	c.1333_1334insCGC	p.A445_P446insP	26%	15%	No

Note: PA: purine analog

Supplementary Table 3. Copy number alterations identified in classical Hairy Cell Leukemia (cHCL).

Sample ID	Case Cohort	Gene	Chromosomal Position	Copy Number Status	BRAF VAF	cHCL (%)	Paired Normal	FISH Positive
OA-hcl-001-P	Relapse/Refractory	*SMO*	7q32.1	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*BRAF*	7q34	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*EPHB6*	7q33-q35	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*EZH2*	7q35-q36	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*MET*	7q31	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*GRM3*	7q21.1-q21.2	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*CDK6*	7q21-q22	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*EPHB4*	7q22	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*PIK3CG*	7q22	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*CRKL*	22q11.21	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*ARID1A*	1p36.1-p35	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*NTRK1*	1q21-q22	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*NF1*	17q11.2	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*TP53*	17p13.1	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*MAPK1*	22q11.2	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*SMARCB1*	22q11.23	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*CHEK2*	22q12.1	Loss	97.5%	100%	No	No
OA-hcl-001-P	Relapse/Refractory	*NF2*	22q12.2	Loss	97.5%	100%	No	No
OA-hcl-003-P	Relapse/Refractory	*SMO*	7q32.1	Loss	75.7%	67%	Yes	Yes
OA-hcl-003-P	Relapse/Refractory	*BRAF*	7q34	Loss	75.7%	67%	Yes	Yes
OA-hcl-003-P	Relapse/Refractory	*RB1*	13q14.2	Loss	75.7%	67%	Yes	Yes
OA-hcl-003-P	Relapse/Refractory	*DIS3*	13q21.32	Loss	75.7%	67%	Yes	Yes
OA-hcl-006-P	Relapse/Refractory	*KLF6*	10p15	Loss	37.6%	80%	Yes	No
OA-hcl-006-P	Relapse/Refractory	*GATA3*	10p15	Loss	37.6%	80%.	Yes	No
OA-hcl-006-P	Relapse/Refractory	*BRCA2*	13q12-q13	Loss	37.6%	80%	Yes	No
OA-hcl-006-P	Relapse/Refractory	*RB1*	13q14.2	Loss	37.6%	80%	Yes	No
OA-hcl-006-P	Relapse/Refractory	*DIS3*	13q21.32	Loss	37.6%	80%	Yes	No
OA-hcl-006-P	Relapse/Refractory	*ERCC5*	13q22-q34	Loss	37.6%	80%	Yes	No
OA-hcl-006-P	Relapse/Refractory	*IRS2*	13q34	Loss	37.6%	80%	Yes	No
OA-hcl-010-P	Relapse/Refractory	*SMO*	7q32.1	Loss	79.5%	72%	Yes	Yes
OA-hcl-010-P	Relapse/Refractory	*BRAF*	7q34	Loss	79.5%	72%	Yes	Yes
OA-hcl-010-P	Relapse/Refractory	*EPHB6*	7q33-q35	Loss	79.5%	72%	Yes	Yes
OA-hcl-010-P	Relapse/Refractory	*EZH2*	7q35-q36	Loss	79.5%	72%	Yes	Yes
OA-hcl-010-P	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	79.5%	72%	Yes	Yes
OA-hcl-012-P	Relapse/Refractory	*SMO*	7q32.1	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	BRAF	7q34	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*EPHB6*	7q33-q35	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*EZH2*	7q35-q36	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*MET*	7q31	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*GRM3*	7q21.1-q21.2	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*CDK6*	7q21-q22	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*EPHB4*	7q22	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*PIK3CG*	7q22	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*WNK1*	12p13.3	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*CCND2*	12p13	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*ETV6*	12p13	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*PIK3C2G*	12p12	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*GLI3*	7p13	Loss	77.0%	70%	No	Yes
OA-hcl-012-P	Relapse/Refractory	*EGFR*	7p12	Loss	77.0%	70%	No	Yes
OA-hcl-016-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	2.8%	60%	Yes	No
OA-hcl-017-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	0.6%	80%	Yes	Yes
OA-hcl-017-P	Relapse/Refractory	*RB1*	13q14.2	Loss	0.6%	80%	Yes	Yes
OA-hcl-017-P	Relapse/Refractory	*DIS3*	13q21.32	Loss	0.6%	80%	Yes	Yes
OA-hcl-020-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	47.4%	70%	No	No
OA-hcl-021-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	43.6%	61%	Yes	No
OA-hcl-023-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	0.3%	98%	Yes	No
OA-hcl-026-P	Relapse/Refractory	*MYCN*	2p24.3	Loss	4.9%	20%	No	No
OA-hcl-048-P	Relapse/Refractory	*SMO*	7q32.1	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*BRAF*	7q34	Loss	77.3%	80%	No	No

OA-hcl-048-P	Relapse/Refractory	*EPHB6*	7q33-q35	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*EZH2*	7q35-q36	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*MET*	7q31	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*GRM3*	7q21.1-q21.2	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*CDK6*	7q21-q22	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*EPHB4*	7q22	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*PIK3CG*	7q22	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*MAGI2*	7q21	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*FLCN*	17p11.2	Loss	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*IL7R*	5p13	Gain	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*RICTOR*	5p13.1	Gain	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*MAP3K1*	5q11.2	Gain	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*PLK2*	5q12.1-q13.2	Gain	77.3%	80%	No	No
OA-hcl-048-P	Relapse/Refractory	*PIK3R1*	5q13.1	Gain	77.3%	80%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*RUNX1*	21q22	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*ERG*	21q22	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*TMPRSS2*	21q22	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*U2AF1*	21q22	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*ICOSLG*	21q22	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*GPS2*	17p13	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*TP53*	17p13	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*ALOX12B*	17p13	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*AURKB*	17p13	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*MAP2K4*	17p12	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*NCOR1*	17p12	Loss	35.2%	18%	No	No
OA-hcl-503-P	Relapse/Refractory and PA Refractory	*FLCN*	17p11	Loss	35.2%	18%	No	No
OA-hcl-504-P	Treatment Naïve	*RUNX1*	21q22	Loss	44%	86%	No	No
OA-hcl-504-P	Treatment Naïve	*ERG*	21q22	Loss	44%	86%	No	No
OA-hcl-504-P	Treatment Naïve	*TMPRSS2*	21q22	Loss	44%	86%	No	No
OA-hcl-504-P	Treatment Naïve	*U2AF1*	21q22	Loss	44%	86%	No	No
OA-hcl-504-P	Treatment Naïve	*ICOSLG*	21q22	Loss	44%	86%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*GSK3B*	3q13	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*GATA2*	3q21	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*EPHB1*	3q22	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*PIK3CB*	3q22	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*FOXL2*	3q22	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*ATR*	3q23	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*PIK3CA*	3q26	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*SOX2*	3q26	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*DCUN1D1*	3q26	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*MAP3K13*	3q27	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*EIF4A2*	3q27	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory	*BCL6*	3q27	Gain	92.1%	96%	No	No

	and PA Refractory							
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*TP63*	3q28	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*HGF*	7q21	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*CDK6*	7q21	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*PIK3CG*	7q22	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*MET*	7q31	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*SMO*	7q32	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*BRAF*	7q34	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*EZH2*	7q36	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*KMT2C (MLL3)*	7q36	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*XRCC2*	7q36	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*RHEB*	7q36	Loss	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*RNF43*	17q22	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*RAD51C*	17q22	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*PPM1D*	17q23	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*BRIP1*	17q23	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*CD79B*	17q23	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*AXIN2*	17q24	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*PRKAR1A*	17q24	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*SOX9*	17q24	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*H3F3B*	17q25	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*SRSF2*	17q25	Gain	92.1%	96%	No	No
OA-hcl-508-P	Relapse/Refractory and PA Refractory	*RPTOR*	17q25	Gain	92.1%	96%	No	No
OA-hcl-509-P	Treatment Naïve	*CARD11*	7p22	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*PMS2*	7p22	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*RAC1*	7p22	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*ETV1*	7p21	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*INHBA*	7p14	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*IKZF1*	7p12	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*EGFR*	7p11	Gain	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*HGF*	7q21	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*CDK6*	7q21	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*PIK3CG*	7q22	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*MET*	7q31	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*SMO*	7q32	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*BRAF*	7q34	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*EZH2*	7q36	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*KMT2C (MLL3)*	7q36	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*XRCC2*	7q36	Loss	88.0%	74%	No	No
OA-hcl-509-P	Treatment Naïve	*RHEB*	7q36	Loss	88.0%	74%	No	No
OA-hcl-510-P	Treatment Naïve	*ARID1A*	1p36	Loss (Focal Deletion)	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*PIK3CG*	7q22	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*MET*	7q31	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*SMO*	7q32	Loss	81.0%	47%	No	No

OA-hcl-510-P	Treatment Naïve	*BRAF*	7q34	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*EZH2*	7q36	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*RHEB*	7q36	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*KMT2C (MLL3)*	7q36	Loss	81.0%	47%	No	No
OA-hcl-510-P	Treatment Naïve	*XRCC2*	7q36	Loss	81.0%	47%	No	No
OA-hcl-511-P	Treatment Naïve	*BARD1*	2q35	Loss (Focal Deletion)	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*HGF*	7q21	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*PIK3CG*	7q22	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*MET*	7q31	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*SMO*	7q32	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*BRAF*	7q34	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*EZH2*	7q36	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*RHEB*	7q36	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*KMT2C (MLL3)*	7q36	Loss	71.0%	68%	No	No
OA-hcl-511-P	Treatment Naïve	*XRCC2*	7q36	Loss	71.0%	68%	No	No
OA-hcl-517-P	Treatment Naïve	*NKX3-1*	8p21	Loss	39.7%	44%	No	No
OA-hcl-517-P	Treatment Naïve	*FGFR1*	8p11	Loss	39.7%	44%	No	No
OA-hcl-518-P	Treatment Naïve	*H3F3A*	1q42	Loss	42.4%	68%	No	No
OA-hcl-518-P	Treatment Naïve	*PARP1*	1q42	Loss	42.4%	68%	No	No
OA-hcl-518-P	Treatment Naïve	*HIST3H3*	1q42	Loss	42.4%	68%	No	No
OA-hcl-518-P	Treatment Naïve	*FH*	1q43	Loss	42.4%	68%	No	No
OA-hcl-518-P	Treatment Naïve	*AKT3*	1q44	Loss	42.4%	68%	No	No
OA-hcl-522-P	Treatment Naïve	*CARD11*	7p22	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*PMS2*	7p22	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*RAC1*	7p22	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*ETV1*	7p21	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*INHBA*	7p14	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*IKZF1*	7p12	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*EGFR*	7p11	Gain	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*CDK6*	7q21	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*PIK3CG*	7q22	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*MET*	7q31	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*SMO*	7q32	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*BRAF*	7q34	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*EZH2*	7q36	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*RHEB*	7q36	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*KMT2C (MLL3)*	7q36	Loss	46.2%	18%	No	No
OA-hcl-522-P	Treatment Naïve	*XRCC2*	7q36	Loss	46.2%	18%	No	No

Note: PA: purine analog

Supplementary Table 4. Mutations identified in variant Hairy Cell Leukemia (vHCL).

Case	Case Cohort	Gene	Genomic Coordinates	Genomic Variant	Amino Acid Variant	VAFs	vHCL (%)	Paired Normal
OA-hcl-532-T	Relapse/Refractory	*MAP2K1*	chr15: 66727433	c.150_173delTGAGGCCTTTCTTACCCAGAAGCA	p.E51_Q58del	22%	100%	No
OA-hcl-532-T	Relapse/Refractory	*U2AF1*	chr21:44514780	c.467G>A	p.R156H	46%	100%	No
OA-hcl-534-T	Relapse/Refractory	*TP53*	chr17:7578413	c.517G>A	p.V173M	4%	40%	Yes
OA-hcl-534-T	Relapse/Refractory	*KDM6A*	chrX:44969405	c.4087C>T	p.R1363X	11%	40%	Yes
OA-hcl-534-T	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151878973	c.5972C>T	p.S1991L	5%	40%	Yes
OA-hcl-535-T	Relapse/Refractory	*MAP2K1*	chr15:66729153	c.361T>A	p.C121S	46%	80%	No
OA-hcl-535-T	Relapse/Refractory	*TP53*	chr17:7577037	c.900_901insNN	p.P301*fs**44	90%	80%	No
OA-hcl-535-T	Relapse/Refractory	*ARID1B*	chr6:57100396	c.1333_1334insCGC	p.A445_P446insP	55%	80%	No
OA-hcl-535-T	Relapse/Refractory	*CEBPA*	chr19:33792731	c.584_589delACCCGC	p.H195_P196del	30%	80%	No
OA-hcl-535-T	Relapse/Refractory	*ERCC2*	chr19:45867494	c.813_814insTC	p.R272*fs**63	41%	80%	No
OA-hcl-536-T	Relapse/Refractory	*FBXW7*	chr4:153247289	c.1513C>T	p.R505C	30%	10%	Yes
OA-hcl-536-T	Relapse/Refractory	*CARD11*	chr7:2976810	c.1202A>T	p.D401V	28%	10%	Yes
OA-hcl-536-T	Relapse/Refractory	*CREBBP*	chr16:3807818	c.3601G>T	p.G1201X	26%	10%	Yes
OA-hcl-536-T	Relapse/Refractory	*DDX3X*	chrX:41205625	c.1459T>A	p.F487I	64%	10%	Yes
OA-hcl-537-T	Relapse/Refractory	*TP53*	chr17:7577096	c.842A>G	p.D281G	89%	86%	No
OA-hcl-537-T	Relapse/Refractory	*PBRM1*	chr3:52643542	c.2354T>G	p.L785R	37%	86%	No
OA-hcl-537-T	Relapse/Refractory	*MSH3*	chr5:79950724	c.178_179insCCGCAGCGC	p.A60_A61insAAP	36%	86%	No
OA-hcl-537-T	Relapse/Refractory	*FUBP1*	chr1:78430834	c.554delA	p.N185*fs*	7%	86%	No
OA-hcl-538-T	Relapse/Refractory	*CCND3*	chr6: 41903701	c.855dupA	p.D286*fs*	28%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*CCND3*	chr6:41903745	c.811delC	p.R271*fs*	7%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*KMT2C (MLL3)*	chr7:151860536	c.10126C>T	p.Q3376X	6%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*TERT*	chr5:1295250	Promoter 5'Flank (NA)	NA	43%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*KDM5C*	chrX:53250049	c.200C>T	p.P67L	38%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*FGF12*	chr3:192125856	c.157C>T	p.R53C	45%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*MSH3*	chr5:79950724	c.178_179insCCGCAGCGC	p.A60_A61insAAP	55%	60%	Yes
OA-hcl-538-T	Relapse/Refractory	*NKX2-1*	chr14:36986875	c.813_814insGGCGGGGGC	p.T272_G273insGGG	20%	60%	Yes
OA-hcl-539-T	Relapse/Refractory	*MAP2K1*	chr15:66727451	c.167A>C	p.Q56P	3%	20%	No
OA-hcl-539-T	Relapse/Refractory	*CD36*	chr7:80302672	c.1202_1205delTATT	p.V401*fs*	44%	20%	No

Supplementary Table 5. Copy number alterations identified in variant Hairy Cell Leukemia (vHCL).

Sample ID	Case Cohort	Gene	Chromosomal Position	Copy Number Status	vHCL (%)	Paired Normal	Clinical FISH Positive
OA-hcl-532-T	Relapse/Refractory	*CARD11*	7p22	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*PMS2*	7p22	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*RAC1*	7p22	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*ETV1*	7p21	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*INHBA*	7p14	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*IKZF1*	7p12	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*EGFR*	7p11	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*HGF*	7q21	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*CDK6*	7q21	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*PIK3CG*	7q22	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*MET*	7q31	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*SMO*	7q32	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*BRAF*	7q34	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*EZH2*	7q36	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*RHEB*	7q36	Loss	100%	No	No
OA-hcl-532-T	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	100%	No	No
OA-hcl-535-T	Relapse/Refractory	*VHL*	3p25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*RAF1*	3p25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*TGFBR2*	3p24	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MLH1*	3p22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MYD88*	3p22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*CTNNB1*	3p22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*SETD2*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*RHOA*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MST1*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MST1R*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*BAP1*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PBRM1*	3p21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MITF*	3p13	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*FOXP1*	3p13	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*RYBP*	3p13	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*SHQ1*	3p13	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PNRC1*	6q15	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*EPHA7*	6q16	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PRDM1*	6q21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*FYN*	6q21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*ROS1*	6q22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*IFNGR1*	6q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*TNFAIP3*	6q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*LATS1*	6q25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*ESR1*	6q25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*ARID1B*	6q25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PARK2*	6q26	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MET*	7q31	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*SMO*	7q32	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*BRAF*	7q34	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*EZH2*	7q36	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*RHEB*	7q36	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*TET1*	10q21	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*BMPR1A*	10q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PTEN*	10q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*SUFU*	10q24	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*TCF7L2*	10q25	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*FGFR2*	10q26	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*PAK1*	11q13	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*EED*	11q14	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MRE11A*	11q21	Loss	80%	No	No

OA-hcl-535-T	Relapse/Refractory	*PGR*	11q22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*YAP1*	11q22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*BIRC3*	11q22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*ATM*	11q22	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*SDHD*	11q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*MLL*	11q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*CBL*	11q23	Loss	80%	No	No
OA-hcl-535-T	Relapse/Refractory	*CHEK1*	11q24	Loss	80%	No	No
OA-hcl-536-T	Relapse/Refractory	*MET*	7q31	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*SMO*	7q32	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*BRAF*	7q34	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*EZH2*	7q36	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*RHEB*	7q36	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*SYK*	9q22	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*FANCC*	9q22	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*PTCH1*	9q22	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*TGFBR1*	9q22	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*KLF4*	9q31	Loss	10%	Yes	No
OA-hcl-536-T	Relapse/Refractory	*CIC*	19q13	Loss	10%	Yes	No
OA-hcl-537-T	Relapse/Refractory	*TNFRSF14*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*ERRFI1*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PIK3CD*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MTOR*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*SPEN*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*SDHB*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*ARID1A*	1p36	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*STK40*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CSF3R*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MYCL1*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MPL*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MUTYH*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PIK3R3*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RAD54L*	1p34	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CDKN2C*	1p32	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*JUN*	1p32	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*JAK1*	1p31	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NEGR1*	1p31	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*FUBP1*	1p31	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*BCL10*	1p22	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NRAS*	1p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*VTCN1*	1p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*FAM46C*	1p12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*VHL*	3p25	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RAF1*	3p25	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*TGFBR2*	3p24	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MLH1*	3p22	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MYD88*	3p22	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CTNNB1*	3p22	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*SETD2*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RHOA*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MST1*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MST1R*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*BAP1*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PBRM1*	3p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NKX3-1*	8p21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*GNAQ*	9q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NTRK2*	9q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MEN1*	11q13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*KDM5A*	12p13	Gain	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RAD52*	12p13	Gain	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CCND2*	12p13	Gain	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*ETV6*	12p13	Loss (Focal Deletion)	86%	No	No

OA-hcl-537-T	Relapse/Refractory	*CDKN1B*	12p13	Loss (Focal Deletion)	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PIK3C2G*	12p12	Loss (Focal Deletion)	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*KRAS*	12p12	Gain	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*GREM1*	15q13	Loss (Focal Deletion)	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RAD51*	15q15	Loss (Focal Deletion)	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*TP53*	17p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*ALOX12B*	17p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*AURKB*	17p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MAP2K4*	17p12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NCOR1*	17p12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*FLCN*	17p11	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*NF1*	17q11	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*SUZ12*	17q11	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RAD51D*	17q12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CDK12*	17q12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*ERBB2*	17q12	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RARA*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*STAT5B*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*STAT5A*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*STAT3*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*BRCA1*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MAP3K14*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*HOXB13*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*SPOP*	17q21	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*RNF43*	17q22	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*STK11*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*TCF3*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*DOT1L*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*GNA11*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*MAP2K2*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PTPRS*	19p13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*CIC*	19q13	Loss	86%	No	No
OA-hcl-537-T	Relapse/Refractory	*PPP2R1A*	19q13	Loss	86%	No	No
OA-hcl-538-T	Relapse/Refractory	*SMO*	7q32	Loss	60%	Yes	No
OA-hcl-538-T	Relapse/Refractory	*BRAF*	7q34	Loss	60%	Yes	No
OA-hcl-538-T	Relapse/Refractory	*EZH2*	7q36	Loss	60%	Yes	No
OA-hcl-538-T	Relapse/Refractory	*RHEB*	7q36	Loss	60%	Yes	No
OA-hcl-538-T	Relapse/Refractory	*KMT2C (MLL3)*	7q36	Loss	60%	Yes	No